

Optical imaging contrast agents

Field of the invention

5 The present invention provides contrast agents for optical imaging of vulnerable atherosclerotic plaque in patients. The contrast agents may be used in diagnosis of vulnerable atherosclerotic plaque, for follow up of progress in disease development, and for follow up of treatment of vulnerable atherosclerotic plaque.

10 The present invention also provides new methods of optical imaging of vulnerable atherosclerotic plaque in patients, for diagnosis and for follow up of disease development and treatment of vulnerable atherosclerotic plaque.

Description of related art

15 Cardiovascular diseases kill about 15 million people in the world each year. Several of these die suddenly of a first myocardial infarction or cardiac arrest without any symptoms or diagnosis of coronary artery disease. Very many of these sudden deaths are caused by unstable or vulnerable plaque that suddenly blocks blood flow in critical arteries in the brain, the lungs or the heart. The rupture of vulnerable plaques contributes to about 75% of all myocardial infarctions and strokes. Today,
20 no general diagnostic method is available for detection or characterisation of such plaques, but several methods have been suggested in the prior art. These vulnerable plaques consist of a lipid core (free and esterified cholesterol), macrophages, collagen and other matrix proteins.

25 Several methods have been suggested for detection of vulnerable atherosclerotic plaque. Some of these are drawn to techniques based on measurement of temperature. See e.g. US 6,615,071 (The University of Texas) which suggests to detect vulnerable atherosclerotic plaque based on identification of regions with elevated temperature. US 6,579,243 (SciMed Life Systems) describes a catheter with
30 thermal sensor for detection of vulnerable plaque.

Other methods are directed to in vitro diagnosis based on samples from a patient. See e.g. US 6,524,795 (Interleukin Genetics) which relates to diagnosis of plaque based on a nucleic sample from the patient and detection of IL-1 genotype patterns.

US 6,375,925 (University of California) suggests non-invasive imaging of atherosclerotic plaque using labelled monoclonal antibodies which bind oxidation specific epitopes like oxidized LDL.

5 Further methods have been described using different diagnostic imaging modalities, but without use of a contrast agent. See e.g. US 6,262,575 (Siemens) which describes a method of MR imaging of plaque identifying fat. No contrast agents are involved. US 5,217,456 (PDT Cardiovascular) describes a method to differentiate healthy tissue from atherosclerotic plaque based on fluorescence signals. This is an
10 intravascular optical imaging method without use of contrast agents.

Further methods have been described using light for detection of atherosclerotic plaque without use of any contrast agents. US 5,275,594 (C.R. Bard) describes a method to distinguish between atherosclerotic plaque and normal tissue by analysing
15 photoemissions from a target site. US 5,197,470 (Eastman Kodak) describes a method and instrument using near IR to discriminate between healthy tissue and diseased tissue. The method might be used for diagnosis of plaque. US 5,046,501 (Wayne State University) describes a method of identifying atherosclerotic plaque versus viable tissue using light with wavelength between 350 and 390 nm.

20 Methods directed to in vivo imaging using radiolabelled contrast agents have been described. See e.g. US 5,976,496 (Diatide) describes labelled somatostatin analogs for imaging cardiovascular disease. The core of the invention is radio-labelled compounds. Fluorescent labelling is mentioned. US 5,026,537 (Centocor) describes
25 a method for imaging of atherosclerotic plaque using radio-labelled monoclonal antibodies that are specific for activated platelets or activated endothelial cells.

Vulnerable atherosclerotic plaque is still a challenge to diagnose and treat. There is a need for improved diagnostic methods, especially for diagnosis of vulnerable
30 atherosclerotic plaque in an early stage with good reliability. We have surprisingly discovered that the use of optical imaging methods with new contrast agents fulfil these requirements.

Summary of the invention

35 The present invention provides an optical imaging contrast agent with affinity for an abnormally expressed biological target associated with vulnerable atherosclerotic plaque.